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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,448	10/27/2003	Kathleen C.M. Campbell	STU 7398	8896

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SENNIGER POWERS LLP
100 NORTH BROADWAY
17TH FLOOR
ST LOUIS, MO 63102

EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
11/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

Office Action Summary	Application No.	Applicant(s)	
	10/694,448	CAMPBELL, KATHLEEN C.M.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7-33,35,36 and 38-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,3-5,7-17 and 23-32* is/are allowed.

6)☒ Claim(s) *18-22,33,35,36 and 38-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 7/28/2008, are acknowledged and entered. Claims 1, 3-5, 7-33, 35-36, and 38-45 are pending and under examination.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 41 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention regarding "said anti-tumor platinum-coordination compound", is **withdrawn** in light of Applicant's amendments.

Claim Rejections - 35 USC § 112 – 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-22 are again rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for topically applying an otoprotective agent to the round window membrane of a patient, does not reasonably provide enablement for orally or parenterally administering an otoprotective agent to the round window membrane of a patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.

In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

It is not clear how one could orally administer an otoprotective agent to the round window membrane of a patient. Oral administration involves ingestion of an active agent through the alimentary canal. However, the round window membrane of a patient is a membrane

associated with the connection between the inner ear and the middle ear. As such, it is unclear how one could administer a compound *via* oral administration to the round window membrane of a patient. Applicants have provided no guidance or direction with respect to how one skilled in the art could administer an otoprotective agent to the round window membrane of patient via oral administration of said otoprotective agent. In fact, Applicants only disclose in the specification topical administration to the round window membrane of the ear (page 45, lines 21-25).

Applicant's arguments have been carefully considered but they are not persuasive. Applicant argues that the phrase "to the round window membrane" modifies topically only and does not modify parenterally or orally. However, claim 18 recites the limitation, "The method of claim 1, wherein said otoprotective agent is administered parenterally, orally or topically to the round window membrane of said patient". Thus, in the absence of a comma between "orally" and "topically", the claims are reasonably construed to mean that administration to the round window membrane of the patient is "orally or topically". This rejection might be overcome by placing a comma between the words "orally" and "topically" (e.g., "The method of claim 1, wherein said otoprotective agent is administered parenterally, orally, or topically to the round window membrane of said patient".

Accordingly, the rejection of claims 18-22 is maintained for the reasons of record and as reiterated above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33, 35, 36, and 38-45 are rejected under 35 U.S.C. 102(b) as being anticipated by **Furuno *et al.*** (USP No. 3,962,429; Issued June 8, 1976).

The instant claims recite methods of reducing ototoxicity in patients undergoing treatment with an aminoglycoside antibiotic comprising administering an effective amount of methionine.

Furuno *et al.* teach methods of reducing side effects (*e.g.*, renal and 8th nerve toxicities) of aminoglycoside antibiotics comprising administering a glucosaccharic acid as well as the aminoglycoside antibiotic to a patient (Abstract). In the methods of the invention, the glucosaccharic acid may be administered simultaneously with or at different times from the aminoglycoside antibiotic (col. 2, lines 22-25).

With respect to methionine as recited in the instant claims as an otoprotective agent, Furuno *et al.* teach that glucosaccharic acids are not stable so methionine is preferably added to parenteral injections containing glucosaccharic acids as a stabilizer (col. 2, lines 56-58).

With respect to an otoprotective agent that "comprises methionine", Furuno *et al.* teach compositions comprising methionine, which is reasonably interpreted as at least a racemic mixture of D and L isomers. Such a mixture "comprises" L-methionine as recited in claim 36.

With respect to the timing of administration as recited in claims 41-45, it is noted that all of these claims encompass simultaneous administration, which is clearly taught in Furuno *et al.*

The reference thus teaches administration of compositions "comprising" administration of an effective amount of methionine to patients undergoing treatment with an aminoglycoside antibiotic as recited in the instant claims. A composition comprising a glucosaccharic acid and methionine as taught in Furuno *et al.*, administered to a patient taking an aminoglycoside antibiotic, meets the limitations of the instant claims.

With respect to the claimed reduction in ototoxicity, it is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a

prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

Though Furuno *et al.* does not expressly teach reducing the incidence of ototoxicity in a patient undergoing treatment with an aminoglycoside antibiotic as a result of the administration of a composition comprising a glucosaccharic acid and methionine, the administration of the same compound(s) as claimed to the same host as claimed is considered to necessarily have the claimed effect of reducing ototoxicity on the subject being treated, whether expressly recognized by Furuno *et al.* or not. Products of identical chemical composition cannot exert mutually exclusive properties when administered under the same circumstances or, in the present case, the same host. Please reference MPEP §2112.

The explanation of an effect obtained when using a composition cannot confer novelty on a known process if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. In other words, even if the reducing the incidence of ototoxicity effect was not itself recognized as a pharmacological effect of administering the disclosed compositions of Furuno et al. for the disclosed therapeutic purpose(s) discussed therein, such an effect is not considered a new therapeutic application because a known therapeutic effect (i.e., reducing toxicities such as renal and 8th nerve toxicities) and benefit of using this same active compound(s) was already known in the prior art.

Applicant's arguments have been carefully considered but they are not persuasive. Applicant argues that Furano does not teach "treating ototoxicity" but rather teaches treating renal and 8th nerve toxicity. However, the claimed method is not directed to "treating" ototoxicity, but rather to "*reducing the incidence of ototoxicity* in a patient undergoing treatment with an aminoglycoside antibiotic". As such, there is nothing in the recited claim language that requires that a patient have ototoxicity resulting from aminoglycoside antibiotic administration. The claimed method step simply requires the step of "...administering to said patient an effective amount of an otoprotective agent comprising methionine...". The Examiner is interpreting "said patient" to mean a patient being treated with an aminoglycoside antibiotic, which is the same patient recited in Furano. As such, administration of a composition comprising an aminoglycoside antibiotic, a glucosaccharic acid, and methionine (e.g., Example 4 in Furano) to a patient anticipates the instantly claimed methods because a reduction *in the incidence of*

ototoxicity will necessarily occur. This is because the same composition as claimed is being administered to the same patient as claimed. It is not pertinent that not all patients receiving an aminoglycoside antibiotic experience ototoxicity as argued by Applicant because the claims do not recite such a limitation. However, in those patients who would experience ototoxicity resulting from administration of an aminoglycoside antibiotic, the incidence of such ototoxicity would naturally be reduced when the method described in Furano is carried out.

Accordingly, the rejection of claims 33, 35, 36, and 38-45 is maintained for the reasons of record and as reiterated above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of Claims 1, 3-5, 7-17, and 23-32 under 35 U.S.C. § 103(a) as being unpatentable over **Basinger *et al.*** (Toxicology and Applied Pharmacology, 1990, vol. 108, pages 1-15) (cited by Applicant in IDS filed 2/28/2005) is **withdrawn** in view of Applicant's arguments. It is the position of the Examiner that Applicant has indeed demonstrated an unexpected result regarding the administration of methionine to patients treated with a platinum-coordination compound. While Basinger teaches that administration of methionine to rats undergoing CDDP therapy results in a decrease in nephrotoxicity, there is no teaching or suggestion that the rats would have developed ototoxicity or that methionine reduced ototoxicity.

Allowable Subject Matter

Claims 1, 3-5, 7-17, and 23-32 allowable over the prior art of record.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614